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EXAMINER
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ART UNIT	PAPER NUMBER
1812	2

DATE MAILED: 06/22/92

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-24 are pending in the application.
   Of the above, claims 13, 17-24 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-12, 14-16 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____ has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 9-89)

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Restriction to one of the following inventions is required under 35 U.S.C. § 121:

I. Claims 1-12 and 14-16, drawn to cDNA encoding cystic fibrosis transmembrane conductance regulator, vectors, expression and therapeutic compositions, classified in Class 536, subclass 27.

II. Claims 13 and 17-21, drawn to a method of treating cystic fibrosis via gene therapy, classified in Class 435, subclass 69.1.

III. Claims 22-24, drawn to a method for producing antibodies against CFTR, classified in Class 530, subclass 387.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P.

§ 806.05(h)). In the instant case, the product as claimed can be used in a materially different process, such as to study ion conductance.

Inventions I and III are separate and distinct because the cDNA is different in chemical composition and function when compared to immunoglobulins. The method of producing antibodies involves proteins and does not rely on DNA.

Inventions II and III are separate because each Invention is for different methods, each distinct from the other.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

During a telephone conversation with Mark Hofer on May 29, 1992 a provisional election was made with traverse to prosecute Invention I, claims 1-12 and 14-16. Affirmation of this election must be made by applicant in responding to this Office action. Claims 13 and 17-24 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

Claims 3-10 and 14-16 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-45 of copending application Serial No. 07/488307. Although the conflicting claims are not identical, they are not patentably distinct from each other because these Claims all claim the cDNA encoding the CFTR and its expression and therapeutic compositions.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The obviousness-type double patenting rejection is a judicially established doctrine based upon public policy and is

primarily intended to prevent prolongation of the patent term by prohibiting claims in a second patent not patentably distinct from claims in a first patent. In re Vogel, 164 USPQ 619 (CCPA 1970). A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) would overcome an actual or provisional rejection on this ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. § 1.78(d).

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 1 and 2 are provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as that of claims 1 and 7 of copending application Serial No. 07/488307. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claim 15 is rejected under 35 U.S.C. § 101 because the invention as disclosed is inoperative and therefore lacks utility. Claim 15 is for a pharmaceutical composition of either cDNA encoding CFTR or the CFTR protein (see 35 USC 112 rejection below). The Examiner strongly believes that aerosol inhalation of either composition would render the DNA or protein ion channel inactive because once in the airways they would be either degraded by DNAses or proteases or not be incorporated into cell membrane, and thereby the ion channel would be ineffective.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-10 and 14-16 are provisionally rejected under 35 U.S.C. § 102(e) as being anticipated by copending application Serial No. 07/488307.

Copending application Serial No. 07/488307 has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. § 102(e) if patented. This provisional rejection under 35 U.S.C. § 102(e) is based upon a presumption of future patenting of the conflicting copending application.

This provisional rejection under section 102(e) might be overcome either by a showing under 37 C.F.R. § 1.132 that any unclaimed invention disclosed in the copending application was derived from the inventor of this application and is thus not the invention "by another", or by a showing of a date of invention of any unclaimed subject matter prior to the effective U.S. filing date of the copending application under 37 C.F.R. § 1.131.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section

> 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claim 1 is rejected under 35 U.S.C. § 103 as being unpatentable over Riordan et al. (1989). Riordan et al. discloses the cDNA for CFTR gene. This cDNA is 99% identical to that disclosed by the Applicants, with only a single base change and position 1990. The Applicants state on page 13 that their cDNA sequence is markedly different from the cDNA disclosed by Riordan et al. This is not the case because the Applicants admit that they have acquired the Riordan et al. clones from ATCC (page 10) and, in their 1990 paper published in Nature they state that the "DNA sequence analysis of the complete sequence revealed a sequence identical to that reported by Riordan et al., with the exception that the base at position 1990 is C rather that A". Therefore, the cDNA sequence encoding the CFTR gene (Claim 1) is anticipated by Riordan et al. or, since there is a single base difference between these two long sequence obvious to persons of ordinary skill in the art that the two sequences code for the same protein, that is, CFTR.

Claims 11 and 12 are rejected under 35 U.S.C. § 103 as being

unpatentable over Riordan et al. Riordan et al. teach that the basic defect for CF is the decrease in Cl^- ion conductance across epithelial cell membranes and that this defect is probably due to a failure of an outwardly rectifying anion channel to respond to phosphorylation by cAMP-dependent protein kinase A or C. Therefore, the failure of CF-afflicted cells, that is cells that express the defective CFTR gene, to produce a C band in a kinase assay would have been obvious to persons of ordinary skill in the art because these cells do not respond to kinase C (Claim 11). On page 1072, col. 1, Riordan et al. state that the deletion of Phe^{508} in the NBF may prevent proper binding to ATP or the conformational change required for normal CFTR activity. It is well-known in the art that many proteins are activated after glycosylation and folding. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to recognize that the lack of CFTR glycosylation and subsequent conformational change may be why the CFTR is not active because Riordan et al. suggest this as a possibility based on the Phe deletion.

Claims 15 and 16 are rejected under 35 U.S.C. § 103 as being unpatentable over Riordan et al. Riordan et al. teaches that there are two repeated motifs in the cDNA encoding CFTR and they have called these nucleotide binding folds (page 1070, col. 2). Riordan et al. also teaches that the Phe deletion occurs in NFB-1 (page 1071, col. 1), therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made that NBF-1 could be replaced with NBF-2 because these two domains

are similar and Riordan et al. teaches that NBF-1 contains the molecular defect.

Claims 2, 4-6 and 14 are rejected under 35 U.S.C. § 103 as being unpatentable over Riordan et al. as applied to claims 1, 15, and 16 above, and further in view of Sambrook et al. (1989). Riordan et al. cloned the DNA from the region of the CF locus (page 1066, col. 2) to isolate the cDNA encoding the CFTR gene. Riordan et al. do not teach which phages or cosmids that they used to clone the cDNA, probably because cloning is a technique that is well-known and widely used in the art. However, Sambrook et al. teaches that bacteriophage lambda and cosmid vectors are routinely used for cloning DNA (page 9.4). Sambrook et al. also teaches that cosmids serve as vehicles to introduce the recombinant genomes into bacteria where that are propagated as large plasmids (Claim 2). In Chapter 16, Sambrook et al. teach the expression of proteins from cloned genes (pages 16.2+ and 16.30+; Claims 4, 5, 6, and 14). Taken together, it would have been obvious to one of ordinary skill in the art at the time the invention was made to insert the DNA into phages/plasmids and insert the compositions into cells because the cDNA was cloned in a phage or plasmid by Riordan et al. and Sambrook et al. teaches that cDNA can be used to transfect cells.

Claims 3, and 7-10 are rejected under 35 U.S.C. § 103 as being unpatentable over Riordan et al. and Sambrook et al. as applied to claims 1, 2, 4-6, 14 and 16 above, and further in view of Nichols (1988). Nichols (page 189) teaches that "children

with diseases such as sickle cell anemia, cystic fibrosis, thalassemia, and severe combined immune deficiency live longer that they did in the past, but their lives remain bound by restrictions imposed by their illnesses. Somatic cell gene therapy is one of several new therapeutics approaches that may help such children in the future. A child with a life-threatening but reversible genetic disease caused by a defect in a single gene would be treated with the gene's normal counterpart. The normal gene, provided through recombinant DNA technology, would be inserted into a specific tissue in the child's body and would not be passed on to future generations". With the disclosed cDNA sequence by Riordan et al. and the teachings of Sambrook et al. on how to transform eukaryotic cells to express proteins encoded by cDNA, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make a therapeutic composition with the cDNA encoding CFTR. This concept is supported by Nichols who teaches that somatic cell gene therapy in which a product expressed by a normal gene would function in place of the defective gene product would be a viable method of treating cystic fibrosis.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide and enabling disclosure. The specification does not show data demonstrating that CFTR gene therapy for the treatment of CF will work. The specification also does not discuss the aerosol administration of the CFTR.

Claims 1-10, 14, and 15 rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 6-10 and 15 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 6, and therein 7-10, the Applicants do not indicate if the cDNA will be administered alone or in a host cell. Claim 15 is dependent on Claim 14, which claims the DNA for CFTR. It is not clear if the aerosol will contain the cDNA encoding CFTR or the CFTR ion channel itself.

The disclosure is objected to because of the following informalities: mistypes throughout the specification and claims. Appropriate correction is required.

Any inquiry concerning this communication should be directed to Karen Cochrane Carlson, Ph.D. at telephone number (703) 305-7811.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist

whose telephone number is (703) 308-0196.

DAVID L. LACEY
SUPERVISORY PATENT EXAMINER
GROUP 180
6/17/92